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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,935	10/14/2005	Mika Korkeamaki	3505-1018	2662

466 7590 01/11/2008

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EXAMINER	
WOOD, AMANDA P	

ART UNIT	PAPER NUMBER
1657	

MAIL DATE	DELIVERY MODE
01/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/523,935	KORKEAMAKI ET AL.	
	Examiner	Art Unit	
	Amanda P. Wood	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37-57,67 and 68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-57,67 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/05, 5/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Invention I (claims 37-57 and 67-68) in the reply filed on 5 October 2007 is acknowledged.

Claims 37-57 and 67-68 are presented for consideration on the merits.

Claim Objections

Claim 40 is objected to because of the following informalities: In line 1, claim 40 appears to contain the extra word "of" after the word "to." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 37-57 and 67-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 37, Applicant recites the phrase "the difference in intensities of the mean fluorescences of the fluorescent agents is at least about double on a logarithmic scale" in lines 6-8 of step (f). In particular, it is unclear what Applicant means by "at least about double on a logarithmic scale" (i.e., is Applicant

referring to a particular logarithmic scale, and what does Applicant intend to encompass by "at least about double"?).

In claim 49, Applicant recites the phrase "microparticles are further separated from the sample" in lines 2-3. It is unclear what Applicant intends to encompass by "microparticles" (i.e., are microparticles anything which is not a microorganismal cell, or are they something else which Applicant has not defined?). It is unclear from the claim as drafted what Applicant intends for the microparticles to accomplish in the method. For purposes of examination, the Examiner will assume that by "microparticles" and by the claim containing it, that Applicant intends to mean some sort of standard fluorescing particles or beads which are used in flow cytometry for enumeration of cells in a sample.

In claim 55, Applicant recites the phrase "the sample is a sample from a mammal's organism fluid" in lines 2-3. It is unclear what Applicant means by "mammal's organism fluid." Applicant provides no definition in the instant specification for this phrase to clarify its meaning.

In claim 67, Applicant recites the phrase "measuring their portions." It is unclear what Applicant means by "portions" in this phrase (i.e., does Applicant intend to measure the portion of a sample which is made up by a particular microorganism once it has been identified, or does Applicant intend to measure portions of microorganisms which have been stained with the fluorescent agents of the invention, or does Applicant mean something else by this phrase?).

Claim 37 step (f) recites the limitation "the particles" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 41 recites the limitation "the probes" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim 49 recites the limitation "microparticles" in line 2. There is insufficient antecedent basis for this limitation in the claim. In particular, the parent claim, claim 37, provides no support for microparticles, and therefore, claim 49, which is drawn to a step wherein "microparticles are further separated from the sample" lacks antecedent basis for microparticles.

All other claims depend directly or indirectly from rejected claims and are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 37-48, 50-53, 55-57 and 67-68 are rejected under 35 U.S.C. 102(b) as being anticipated by Schut et al (WO 99/10533).

A method is claimed for identifying and for measuring the portion in a sample one or more microorganisms and/or microorganism species.

Schut et al teach a method of measuring *Bifidobacterium* species in fecal samples by labeling the sample with Cy5-labeled Bif probe, a 16S rRNA probe specific

for *Bifidobacterium* species, and also labeling the sample with universal probes, such as FITC-labeled Eub (stains all bacteria), or with general nucleic acid stains such as YOPRO-1, or SYTO 9. Schut et al teach that the samples were then subjected to flow cytometry for fluorescence readings of the FISH procedure to determine cell counts of the desired species. Schut et al teach that that best separation between fluorescent intensities is achieved with Cy5-labeled Bif probe and YOPRO-1 at 10x diluted commercial concentration, which is demonstrated in Figure 5, panel A top and bottom, discussed on page 53 of Schut et al (see, for example, page 36 line 10 to page 37 line 15, and page 53). Schut et al also teach that forward scatter light signal was measured and plotted versus fluorescence intensity for Cy5 labeled with YOPRO-1 (10x dilution) (see, for example, Figure 4 and page 52). Schut et al further teach that flow cytometric analysis was performed using a Becton Dickson FACScalibur equipped with a 15 mW argon laser (488 nm) and a 10 mW red diode laser (635 nm) (see, for example, page 34, lines 10-33).

Furthermore, Schut et al teach that the method described above can be used to quantitatively measure microorganisms present in a sample in addition to identifying the microorganisms present in the sample. In particular, Schut et al teach that the method can be used to quantitatively measure the flora present in human and animal fecal samples. Schut et al further teach that the method is useful for studying the effects of probiotics on intestinal flora in humans and animals, as well as to identify and quantify the presence of microorganisms in wastewater treatment systems, in addition to several

other beneficial uses (see, for example, page 19 lines 19-36, page 20, lines 1-15, and 34 through page 21).

Therefore, the reference is deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 37-53, 55-57 and 67-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schut et al in view of Matsumoto et al (US 5,888,823).

Schut et al is relied upon for the reasons set forth above.

Schut et al do not expressly teach that microparticles are separated from the sample.

Matsumoto et al beneficially teach a standard fluid for flow cytometry which can be used in quality control and calibration of flow cytometers, and which comprises a fluid and particles which stain similarly to the cells being measured in the cytometer, such as bacteria. Matsumoto et al teach that the fluid allows for counting of cells of interest and does not interfere with fluorescence and scattered light intensities of stained cells. Furthermore, Matsumoto et al beneficially teach that the calibrating

particles of the fluid are measured by the flow cytometer using fluorescence and scattered light intensity (see, for example, Abstract and col. 3-6).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods disclosed by Schut et al based upon the beneficial teachings provided by Matsumoto et al, with respect to the art-recognized method of providing a standard fluid containing particles for counting cells in a flow cytometer, as discussed above. Furthermore, Matsumoto et al beneficially teach that bacteria are among the types of cells which can be enumerated using the standard fluid demonstrated and that the fluorescence and light scattering of the cells are not disrupted by the standard, but that the standard can be used as a calibration tool, and therefore, it would have been both obvious and beneficial for the skilled artisan to use the methods taught by Schut et al in combination with the standard fluid of Matsumoto et al so as to provide an accurate method for identifying and enumerating bacteria in samples.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.

Claim 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schut et al in view of Matsumato et al as applied to claims 37-53, 55-57 and 67-68 above, and further in view of Wallner et al (Cytometry 1993).

Schut et al and Matsumato et al are relied upon for the reasons set forth above,

Schut et al and Matsumato et al do not expressly teach a method wherein the at least two light sources are disposed at a distance from each other, signal delay equipment is used to delay measuring signals being created by means of the first and optionally the subsequent light sources.

Wallner et al beneficially teach a method similar to that of Schut et al, wherein bacteria in a sample are identified by fluorescent probes for 16S rRNA. Wallner et al teach a method using a FACStar Plus flow cytometer equipped with two argon lasers to measure forward angle light scatter, right angle light side scatter, and fluorescent intensity of the microbial cells. Wallner et al teach that during two color measurements, the emission light, excited sequentially by the two lasers, was split by the standard half mirror and fed to the respective photomultiplier tube (see, for example, Abstract and page 138).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the methods disclosed by Schut et al based upon the beneficial teachings provided by Matsumoto et al, with respect to the art-recognized method of providing a standard fluid containing particles for counting cells in a flow cytometer, and by Wallner et al, with respect to the art-recognized method using two different light sources for flow cytometry, as discussed above. Furthermore, Wallner et

al beneficially teach that emission light is fed to the appropriate photomultiplier tube upon sequential excitation of the two light sources, and therefore, it would have been both obvious and beneficial for the skilled artisan to use the methods taught by Schut et al in combination with the method of Matsumato et al and Wallner et al so as to perform accurate measurements of the emission light from the sample.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole, was *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the cited references, especially in the absence of evidence to the contrary.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications should be directed to examiner Amanda P. Wood whose telephone number is (571) 272-8141. The examiner can normally be reached on Mon-Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

APW
Examiner
Art Unit 1657

CHRISTOPHER R. TATE
PRIMARY EXAMINER